

REMARKS

Claims 29 and 36 presently appear in this case. No claims have been allowed. The official action of September 26, 2000, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to a method for identifying and producing a molecule which causes modulation of the phosphorylation of the intracellular domain of the 26 kDa TNF by screening for molecules which have such effect and then producing such molecules. Preferably, the molecules are screened by testing for binding to the intracellular domain of the 26 kDa TNF, and then, if the molecule binds, determining whether or not that molecule modulates the phosphorylation thereof.

Please note that the finality of the present rejection is being traversed and it is requested that such finality be withdrawn. See page 6, *infra*.

The examiner states that newly-submitted claims 28 and 35 are directed to an invention that is independent or distinct from the invention originally claimed.

All of the non-elected claims have now been deleted without prejudice toward the continuation of prosecution thereof in a continuing application, thus obviating this restriction requirement.

Claim 29 has been rejected under 35 U.S.C. §112, second paragraph, over the recitation "capable of modulating".

Claim 29 has been now been amended to delete the term "capable of modulating" and instead to state that the molecule causes modulation of the phosphorylation of the

intracellular domain. As the term to which the examiner has objected no longer appears in the claim, this rejection has now been obviated.

Claim 29 has also been rejected under 35 U.S.C. §112, second paragraph, over the recitation of "directly or indirectly".

Claim 29 has now been amended in order to delete the term "directly or indirectly" as suggested by the examiner. Accordingly, this rejection has also now been obviated.

Claim 29 has been rejected under 35 U.S.C. §112, second paragraph, as the claim does not set forth any steps involved in the screening, identification, characterization and production and, thus, it is unclear what method or process applicants are intended to encompass. The examiner states that a claim is indefinite where it merely recites a process without any active positive steps delimiting how this process is actually practiced. The examiner states that this rejection is also applicable to claim 36 insofar as it includes the identification, characterization and production steps. The examiner states that the yeast two-hybrid procedure is not recited in the rejected claims. This rejection is respectfully traversed.

The screening step of claim 29 has now been amended to clarify that it involves testing each molecule to determine if the molecule causes modulation of the phosphorylation of the intracellular domain of the 26 kDa TNF by increasing or decreasing the extent of the phosphorylation. This clarifies exactly how the screening is carried out. Furthermore, step b) of identifying and characterizing has now been eliminated,

thus obviating this part of the rejection. The final step of producing any said molecule which is determined to cause said modulation, remains. However, as the manner of production is not a critical part of the present invention and anyone of ordinary skill in the art, once a particular molecule is found which tests positive in the screen, would know how to produce such a molecule, it should not be necessary to specify any particular means of producing. A claim is not indefinite because one of the steps is broad. The metes and bounds of the claims are exactly set forth by the term "producing", and anyone of ordinary skill in the art would know whether or not they were infringing this claim. Accordingly, the producing step fully complies with the second paragraph of 35 U.S.C. §112 as it particularly points out and distinctly claims that which applicants consider to be their invention.

Reconsideration and withdrawal of this rejection are, therefore, respectfully urged.

Claim 29 has been rejected under 35 U.S.C. §102(b) as being anticipated by Ohta. The examiner states that the claim reads on Ohta because no steps in the screening process are set forth, and the examiner did not consider the term "capable of modulating" to constitute any type of limitation. The examiner states that incorporating the limitations of claim 36 into claim 29 may overcome the rejection. This rejection is respectfully traversed.

Claim 29 has now been amended to specify that the screening step requires testing each molecule to determine if the molecule causes modulation of the phosphorylation of the TNF intracellular domain. The examiner concedes that this is

not done by Ohta. Accordingly, this rejection has also been obviated by the present amendment to the claims.

Reconsideration and withdrawal of this rejection are also respectfully urged.

Claim 36 has been rejected under 35 U.S.C. §101 as not being supported by either a specific or substantial asserted utility or a well-established utility. The examiner states that the claim is drawn to screening for compounds that modulate the intracellular phosphorylation of 26 kDa TNF, but the biological significance of this phosphorylation is unknown. The examiner states that evidence warranting further study is not equivalent to evidence showing the type of utility required by 35 U.S.C. §101 and that in the context of a utility requirement, a patent is not a hunting license. A patent is not a reward for the search, but compensation for its successful conclusion. This rejection is respectfully traversed.

First of all, it is not understood why the examiner has applied this new rejection only to claim 36 and not to claim 29. On its face, it would appear to apply equally to claim 29. It appears that the only reason that the examiner did not include claim 29 in this rejection is because, to have done so, would have required making this rejection non-final as no amendment to claim 29 in applicants' amendment of March 10, 2000, necessitated this new utility rejection. Thus, to the extent that the examiner considers this rejection applicable to claim 29, it is respectfully requested that the finality of the official action of September 26, 2000, be withdrawn as being premature. If the examiner considers this

rejection to be applicable to claim 36 but not to claim 29, then it is requested that the examiner explain how this can be the case in view of the fact that claim 36 is dependent from claim 29 and includes all the limitations of claim 29. If claim 29 has utility, then claim 36 must also have utility. Thus, to the extent that the examiner considers that claim 29 is not subject to this rejection, reconsideration and withdrawal of this rejection are respectfully urged in view of the fact that claim 36 must inherently include the same utility as is possessed by claim 29.

The present case is substantially different from the *Brenner v. Manson* case cited by the examiner. In that case, the claim was directed to a compound whose utility was unknown, and the Supreme Court held that it is an inappropriate disclosure of utility to say that a utility for a new compound will be discovered in the future. Here, however, the claims are directed to method steps. The claims are process claims and not compound claims. The process is effectively a new tool to be used in medical research. The process of the present claims is no more a "hunting license" than was the first claim to the process of PCR or to a method of chromatography. Thus, using the examiner's analogy, a patent on the present claim is not a "hunting license" as the invention here is directed to the method of hunting. A method of hunting should be patentable. We are not claiming that which is found by the hunt (except as may be covered under the Process Patents Amendment Act). Prior to the discoveries of the present inventors, upon which the present invention was made, it was not known that the intracellular domain of the 26

kDa TNF was phosphorylated. Once this was discovered, the present new technique for finding compounds expected to affect the intracellular signaling of this protein was conceived. The method is a useful tool, just as is a method of chromatography.

Furthermore, specific and substantial utilities for compounds modulating phosphorylation of the intracellular domain of the 26 kDa TNF molecule are disclosed at page 6, lines 3-15 of the present specification where it states:

Thus, the phosphorylation of the intracellular domain of the 26 kDa TNF molecules may be involved in the regulation of expression or proteolytic processing of cell-surface TNF, in the modulation of TNF bioactivity, or in the intracellular signaling process mediated by the cell-surface TNF molecules.

The above findings and their related functional significance represent the first disclosure of a control possibility (both in terms of biological activity and amounts) of the cell-surface form of TNF via control of the activity of the intracellular domain of this form of TNF, in particular, via control of the region in this domain which is subject to phosphorylation.

Accordingly, the present invention provides a modulator of the expression, proteolytic processing, bioactivity or intracellular signaling of the 26 kDa cell-surface-bound form of TNF (26 kDa TNF), said modulator being capable of interacting with the intracellular domain of said 26 kDa TNF or with one or more other intracellular effector proteins which interact with said intracellular domain of the 26 kDa TNF.

Reconsideration and withdrawal of this rejection are, therefore, respectfully urged.

Claim 36 has also been rejected under 35 U.S.C. §112, first paragraph. The examiner states that, since the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility, one skilled in the art would not know how to use the claimed invention. This rejection is respectfully traversed.

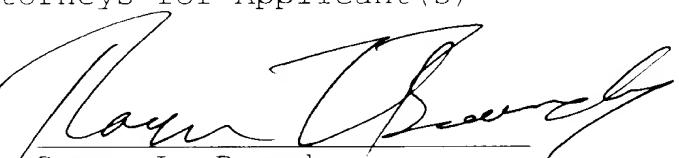
As the 35 U.S.C. §101 rejection must fall for the reasons discussed hereinabove, the 35 U.S.C. §112, second paragraph, how-to-use rejection must fall for the same reasons. Reconsideration and withdrawal of this rejection are also respectfully urged.

It is submitted that all of the claims now present in the case clearly define over the references of record. Reconsideration and allowance are, therefore, earnestly solicited.

Respectfully submitted,

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Version with Markings to Show Changes Made

29 (Amended). A method for identifying and producing a molecule capable of directly or indirectly modulating which causes modulation of the phosphorylation of the intracellular domain of the 26 kDa TNF, comprising:

- a) screening for a molecule capable of modulating molecules by testing each molecule to determine if the molecule causes modulation of the phosphorylation of the intracellular domain of the 26 kDa TNF directly or indirectly, by increasing or decreasing the extent of said phosphorylation; and
- b) identifying and characterizing said molecule; and
- c+b) producing said molecule in substantially isolated and purified form any said molecule which is determined to cause said modulation.

36 (Amended). The method according to claim 29, wherein said screening step comprises testing molecules each molecule for binding to the intracellular domain of the 26 kDa TNF and then determining if a molecule found to bind to the intracellular domain of the 26 kDa TNF in said testing step modulates the phosphorylation of the intracellular domain of the 26 kDa TNF.